

Complexometric titration



- **Objectives of the session**

- Explain principle of Complexometric titration
- Define the terms commonly used
- Elaborate the different EDTA titration methods
- Describe the pharmaceutical application

- **Complexation titration** is a volumetric method based on the formation of a slightly dissociated soluble complex between **cations** and **complex forming reagents**.
 - used to estimate **polyvalent ions** (divalent, trivalent, etc...)
- **Complexes** are compounds formed from combination of metal ions with ligands (complexing agents)
 - **A metal** is an electron deficient species while a ligand is an electron rich.
 - A metal will thus accept electrons from a ligand where *coordination bonds* are formed
 - Electrons forming coordination bonds come solely from ligands

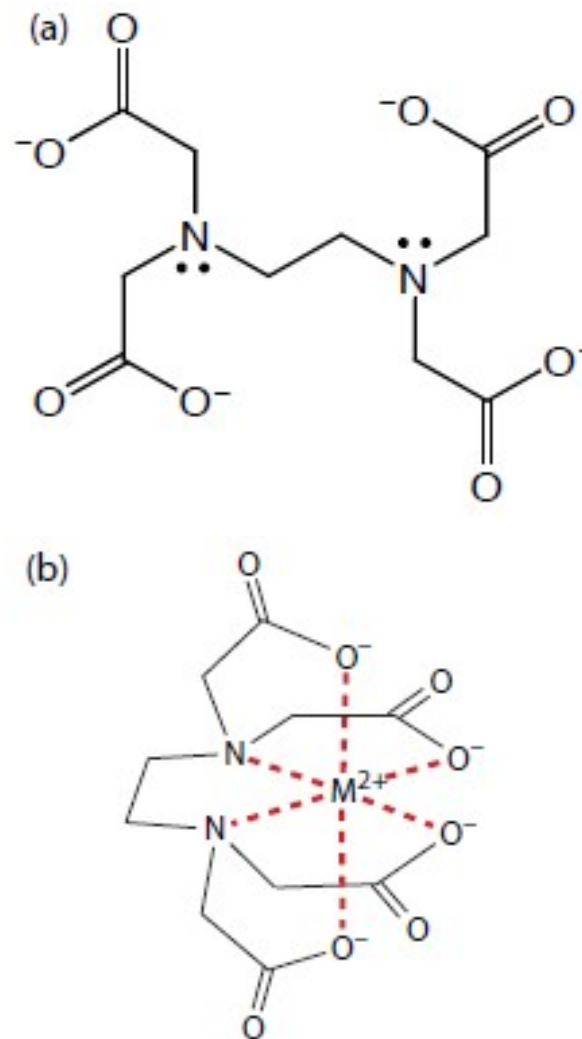
- A **ligand** is called a monodentate if it donates a single pair of electrons (like :NH_3)
 - Forming co-ordination compounds.
- When the ligand contains two or more of the complexing groups, it is called a **chelating agent** and the formed complex, is called a **chelate**
 - Ex. bidentate ligand (like ethylenediamine, $\text{:NH}_2\text{CH}_2\text{CH}_2\text{H}_2\text{N:}$) donates two pairs of electrons
 - Ethylenediamine tetra-acetic acid (EDTA) is a hexadentate ligand

Titration with multidentate complexers

- Multidentate ligands (chelating agents) are more suitable titrants than unidentate ligands because:
 - i) they tend to form 1 : 1 complexes in one step.
 - ii) their reactions with metal ion form chelation, so their complexes are more stable.
- Ethylenediamine tetra-acetic acid (**EDTA**) is the most frequently used chelate in complexometric titrations

EDTA Titrations

- EDTA, is an aminocarboxylic acid
- is a Lewis acid with six binding sites: the four negatively charged carboxylate groups and the two tertiary amino groups
- The resulting metal–EDTA complex forms a very stable cage-like structure around the metal ion.
- The actual number of coordination sites depends on the size of the metal ion, however, all **metal–EDTA complexes have a 1:1 stoichiometry.**



Factors affecting stability of the metal-EDTA complexes

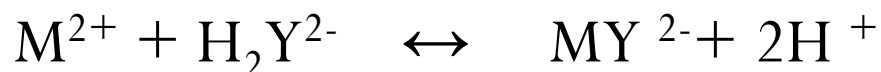
1- Effect of pH

✚ Edetic acid (H_4Y) ionizes in four stages to form

➡ H_3Y^- , H_2Y^{2-} , HY^{3-} , and Y^{4-} species

- Since the actual complexing form of EDTA is Y^{4-} , so the stability of Metal-EDTA chelates depends on the pH of the solution, which makes the form Y^{4-} predominate.

e.g divalent metal – EDTA complex



- The stability of a given chelate (MY^{2-}) increases as the pH increases, because, the liberated H^+ ion will be neutralized in alkaline sol'n., and thus the reaction is shifted to the right → i.e., more complex formation.
- More stable complexes are best formed in alkaline pH.

2- Nature of the metal ion :

- Some **metal**-EDTA chelates are stable in acidic soln., (PH<4)
e.g trivalent cations, Fe^{3+} , Bi^{3+} .
 - Other **metal**-EDTA chelates are stable at pH 4→7
e.g Fe^{2+} , Cu^{2+} , Zn^{2+} , Pb^{2+} .
 - Other chelates are stable at pH>7 e.g Ca^{2+} , Mg^{2+} .
- So, by controlling the pH of the solution, one can improve the selectivity of EDTA.

To do so, titrated solutions are usually buffered at a pH at which the complex is stable and at which the color change of the indicator is clear.

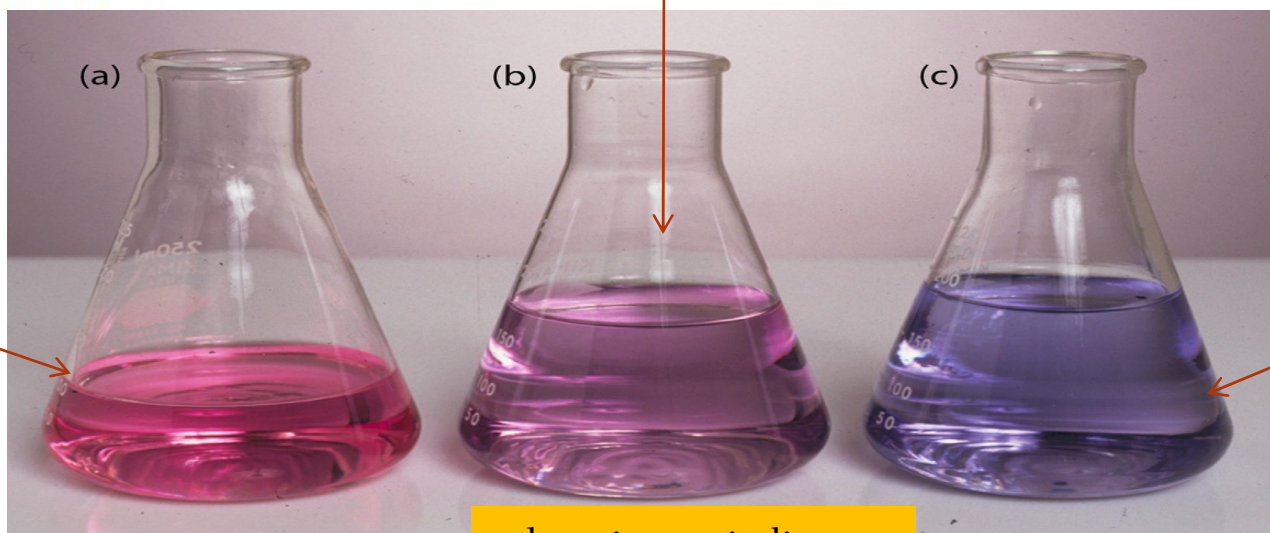
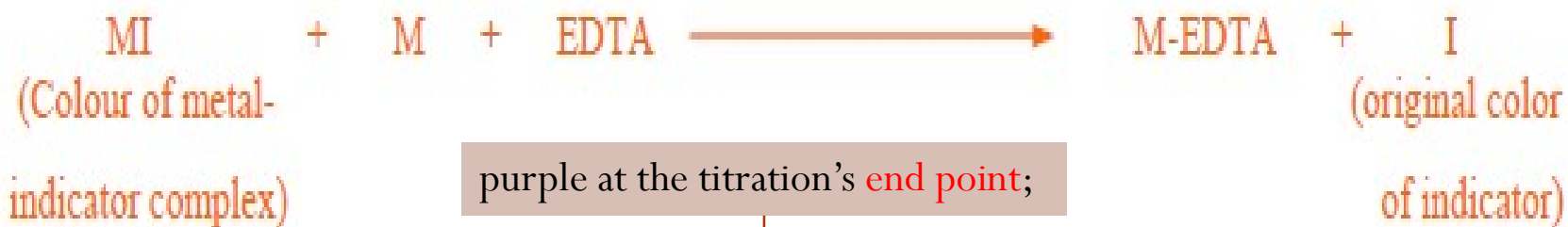
Endpoint Detection

- End point in complexometric titration can be detected by the following two methods:
 - **Chemical indicator**
 - **Instrumental methods of End point detection:**
 - Spectrophotometric detection:
 - Amperometric titration
 - **Potentiometric titration:**

1. Chemical Indicators:

☞ The indicator is a dye which is capable of acting as a chelating agent to give a **dye-metal complex**.

☞ The metal-indicator complex is different in colour from the dye itself and also has a low stability constant than the chelate-metal complex.



calmagite an indicator

Indicator	pH range	Metal ion
calmagite	8.5–11	Ba, <u>Ca</u> , Mg, Zn
eriochrome Blue Black R	8–12	<u>Ca</u> , Mg, Zn, Cu
murexide	6-13	<u>Ca</u> , Ni, Cu
eriochrome Black T	7.5-10.5	Ba, <u>Ca</u> , Mg, Zn
salicylic acid	2-3	Fe

Remark: all ions are 2^{+} , except $\text{Fe } 3^{+}$; Ca = poor endpoint

Methods used in EDTA titration

1. Direct Titration

- A suitable buffer solution and indicator are added to the metal ion solution
- The solution titrated with standard disodium edetate until the indicator just changes colour
- E.g.-calcium gluconate injection, calcium lactate tablets

2. Back Titration

- A measured excess of standard EDTA solution is added, and the excess is back-titrated with standard solution of metal ion, usually magnesium or Zinc chloride (or sulphate)
- EDTA back-titrations are generally used for one of three reasons:
 - (i) reaction kinetics are **too slow for the direct titration** of the analyte;
 - (ii) the metal precipitates at the desired pH;
 - metal ion form an insoluble hydroxide because of high pH required, e.g. Mn forms $\text{Mn}(\text{OH})_2$ precipitation
 - (iii) there is **no suitable chemical indicator** for the direct titration

3. Replacement Titration

- When direct or back titrations do not give sharp end points, the metal may be determined by the displacement of an equivalent amount of Mg or Zn from a less stable EDTA complex
 - e.g. determination of Calcium
 - ➡ **Problem:** Calcium-Eriochrome Black T complex is very weak
 - color change at the end point is vague
 - **direct titration** is impossible
 - ➡ Magnesium-Eriochrome Black T complex is strong
 - endpoint detection for titration of Mg^{2+} with EDTA is good

- Due to the relative strength of complex they form cation replacement titration is practical.
 - Ca-EDTA complex is stronger than Mg-EDTA
 - Mg-EDTA complex is stronger than Mg-Indicator
 - Mg-I complex is stronger than Ca-I complex
- Ca determination is carried out by adding some magnesium sulphate together with the indicator to the calcium solution
 - this mixture is titrated with EDTA
 - the Ca-EDTA complex is formed
 - Mg-indicator complex maintains the typical red color
 - at the endpoint EDTA displaces the indicator from Mg-I complex, color changes to **blue**

Pharmaceutical Application

A. Determination of Pharmaceutical compounds which contain **metal ions** that undergo complexation reactions

i. Inorganic salts: Magnesium sulfate

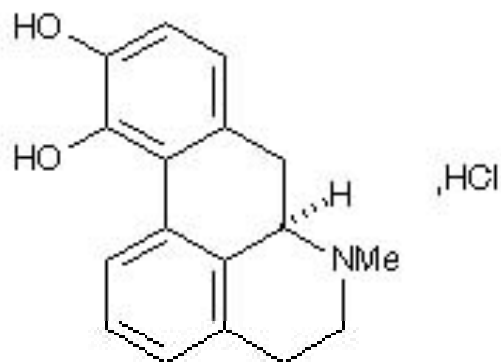
- Magnesium trisilicate
- Zinc Oxide
- Calcium in Ringer's solution
 - a solution of the chlorides of sodium, potassium and calcium

ii. Organic Salts

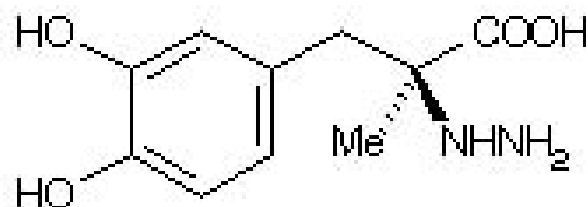
- Calcium Lactate injection
- Calcium Gluconate
- Calcium ascorbate

B. Determination of Pharmaceutical compounds having Chelating properties:

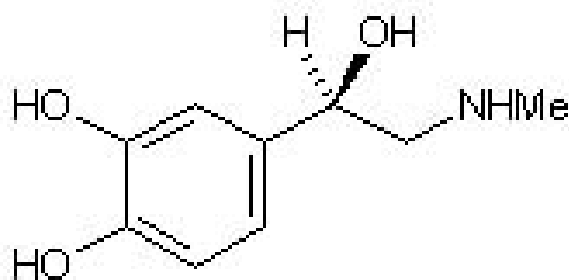
Examples:



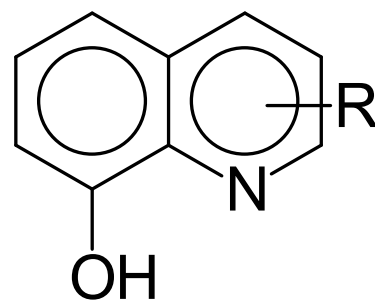
Apomorphine



Carbidopa



Adrenaline



8-Hydroxyquinolines

C. Determination of Hardness of Water

- The operational definition of water hardness is the total concentration of cations in a sample that can form an insoluble complex with soap.
- Although most divalent and trivalent metal ions contribute to hardness, the **two most important metal ions are Ca^{2+} and Mg^{2+} .**
- Hardness is determined by titrating with EDTA at a buffered pH of 10
 - Hardness is reported as mg Ca/L

Practices:

Q1. 35.00 mL of 0.055 M EDTA (an excess) is added to 20.00 mL of 0.625%w/v magnesium chloride (95.2 g/mol) sample solution. The excess EDTA is back-titrated with 12.5 mL of 0.048 M Zinc chloride

- i. calculate the amount of magnesium chloride (in mg) in the sample solution

Answer 126.14 mg

- ii. Calculate the percentage stated content of MgCl_2

Answer: 100.9%

Q2. In your pharmaceutical Analysis laboratory, you assayed calcium gluconate injection (stated as 10 % w/v of calcium gluconate (M.wt = 430.38 g/ mol) by complexometric titration as follows: 2ml of calcium gluconate injection solution was mixed with distilled water to which MgSO_4 , ammonium chloride buffer and Mordant black indicator were added. The resulting solution was titrated with 0.05 M EDTA and 12.13ml was consumed. And For blank titration 3.15 ml of the titrant was consumed

- i. Calculate the content (in mg) of Calcium (40.078gm/mol) in the sample taken for analysis

Answer: 17.995 mg

- ii. Judge the quality of the sample based on BP which describes the acceptable limit as the content of calcium should be 8.5 to 9.4% of the content of calcium gluconate stated on the label

Answer: 8.997%, accepted

The End of Complexation titration!